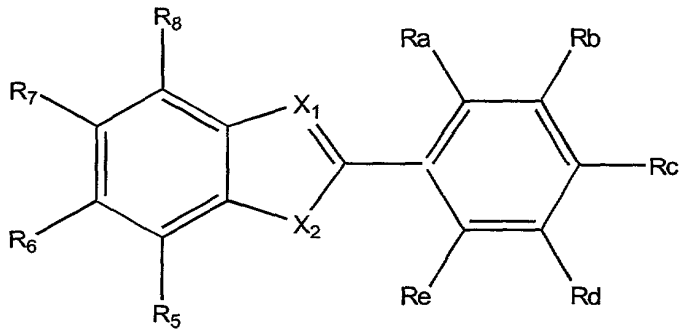
G. Other Embodiments

The features and advantages of the invention are apparent to one of ordinary skill in the art. Based on this disclosure, including the summary, detailed description, background, examples, and claims, one of ordinary skill in the art will be able to make modifications and adaptations to various conditions and usages. These other embodiments are also within the scope of the invention.

What is claimed is:

Claims

1. A compound of formula (I)(B):



wherein

X_1 is CR_1, wherein R_1 is H, halo, cyano, amino, or nitro; and X_2 is NR_3;

R_3 is H, $-SO_2$ (C_{1-6} alkyl), $-SO_2$ phenyl, (C=O)(C_{1-6} alkyl), or -W'Z';

W' is a covalent bond, (C=O), SO_2, or C_{1-6} alkyl;

Z' is C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-8} cycloalkyl, phenyl, or C_{2-6} heterocyclic radical, optionally including in the ring up to 3 additional heteroatoms or moieties independently selected from O, N, NH, S, SO, and SO_2; or Z' is $NR_{13}R_{14}$ where each of R_{13} and R_{14} is independently selected from C_{1-6} alkyl, C_{2-6} alkenyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical;

each of R_5, R_6, R_7 and R_8 is independently H, C_{1-6} alkyl, C_{1-6} alkoxy, halo, nitro, or amino;

one of R_a, R_b, R_c, R_d, and R_e is WZ and the others are independently selected from H, C_{1-6} alkyl, C_{1-6} alkoxy, halo, nitro, and amino;

W is -O-, R_9, O-R_9, NR_{10}, -(CO)(O)R_9, -O (CO)R_9, -(CO)NR_{10}, or -N(R_{10})-CO-R_9, wherein R_9 is C_{1-6} alkylene, C_{2-6} alkynylene, C_{2-6} alkenylene, phenylene, or C_{2-5} heterocyclic bivalent radical, and R_{10} is H, C_{1-6} alkyl, C_{2-6} alkynyl, C_{2-6} alkenyl, phenyl, or C_{2-5} heterocyclic radical;

Z is C_{2-8} heterocyclic radical with at least one basic nitrogen atom in the ring, optionally including in the ring up to 3 additional

heteroatoms or moieties independently selected from O, C=O, N, NH, NG, S, SO, and SO_2, wherein G is R_{15}, COR_{15}, $COOR_{15}$, SO_2R_{15}, SO_2N, CSR_{15}; or Z is $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-6} alkyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical; or $NR_{11}R_{12}$ taken together is a C_{6-8} cycloalkylimino radical; and R_{15} is C_{1-6} alkyl, C_{2-6} alkynyl, C_{2-6} alkenyl, C_{3-7} cycloalkyl, and C_{4-7} cycloalkenyl; each of the above hydrocarbyl or heterocyclic groups being optionally substituted with between 1 and 3 substituents selected from C_{1-3} alkyl, C_{1-3} alkoxy, halo, hydroxy, phenyl, and phenyl(C_{1-3} alkyl); and wherein each of the above heterocyclic groups may be attached to the rest of the molecule by a carbon atom or a heteroatom;
or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.

2. A compound of claim 1, wherein R_3 is H or C_{1-3} alkyl.

3. A compound of claim 1, wherein R_3 is -(C=O)C_{1-6} alkyl.

4. A compound of claim 1, wherein R_3 is -SO_2(C_{1-3} alkyl).

5. A compound of claim 4 wherein R_3 is methylsulfonyl.

6. A compound of claim 1, wherein W' is a covalent bond.

7. A compound of claim 1, wherein W' is SO_2 or (C=O).

8. A compound of claim 1, wherein R_c is WZ.

9. A compound of claim 1, wherein R_b or R_d is WZ.

10. A compound of claim 1, wherein W is ethoxy, propoxy, or butoxy.

11. A compound of claim 1, wherein W is -O-.

12. A compound of claim 1, wherein one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, nitro, and halo; and R_a and R_d are each independently H or methyl.

13. A compound of claim 1, wherein at least two of the following apply: R_c is WZ; W is propoxy or ethoxy; and Z is N-piperidino, 2-(N-methyl)pyrrolidino, or N,N-dimethyl.

14. A compound of claim 1, wherein Z is pyrrolidino, N-methyl-pyrrolidino, pyridyl, thiazoyl, piperidino, or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C $_{1-6}$ alkyl, phenyl, benzyl, C $_{3-6}$ cycloalkyl, and C $_{2-5}$ heterocyclic radical or taken together with the N form a C $_{6-8}$ cycloalkylamino radical.

15. A compound of claim 1, wherein one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, and halo; and R_a and R_d are each independently H or methyl;
W is -O- or C $_{1-3}$ alkoxy;
Z is pyrrolidino, N-methylpyrrolidino, pyridyl, thiazoyl, piperidino, piperazino, N-methylpiperazino,or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C $_{1-2}$ alkyl, phenyl, benzyl, C $_{3-8}$ cycloalkyl, and C $_{2-5}$ heterocyclic radical; each of R_6 and R_7 are each independently H, methyl, methoxy, or ethoxy; each of R_5 and R_8 is H.

16. A compound of claim 15, wherein R_3 is H or -SO_2 (C $_{1-6}$ alkyl).

17. A compound of claim 15, wherein R_3 is SO_2(phenyl) and (C=O)(C_{1-6} alkyl).

18. A compound of claim 15, selected from 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1H-indole, 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1-(methylsulfonyl) -1H-indole, and 2-[4-[3-Piperidinopropoxy]phenyl)-1H-indole;) 2-(4-(3-(4-methylpiperazino)propoxy)-phenyl)indole; and 1-(methylsulfonyl)-2-(4-(3-(4-methylpiperazino)-propoxy)phenyl)indole; or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.

19. A compound of claim 15, selected from 2-[4-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole, and 2-[3-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.

20. A pharmaceutical composition comprising a compound of formula (I)B and a pharmaceutically acceptable carrier.

21. A pharmaceutical composition of claim 20, wherein said compound has a formula wherein: one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, and halo;
R_a and R_d are each independently H or methyl;
W is -O- or C_{1-3} alkoxy;
Z is pyrrolidino, N-methylpyrrolidino, pyridyl, thiazoyl, piperidino, or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-2} alkyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical; and
R_6 and R_7 are each independently H, methyl, methoxy, or ethoxy.

22. A pharmaceutical composition of claim 21, wherein said compound has a formula selected from 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1H-indole; 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1-(methylsulfonyl) -1H-indole; 2-[4-[3-Piperidinopropoxy]phenyl)-1H-indole; 2-[4-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole; 2-[3-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole; 2-(4-(3-(4-methylpiperazino)propoxy)-phenyl)indole; and 1-(methylsulfonyl)-2-(4-(3-(4-methylpiperazino)-propoxy)phenyl)indole; or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.

23. A method for treating disorders mediated by the histamine H_3 receptor in a patient, said method comprising administering to the patient a pharmaceutically effective amount of compound of formula (I)B.

24. A method of claim 23, wherein said compound has a formula wherein: one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, and halo;
R_a and R_d are each independently H or methyl;
W is -O- or C_{1-3} alkoxy;
Z is pyrrolidino, N-methylpyrrolidino, pyridyl, thiazoyl, piperidino, N-methylpiperazino, or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-2} alkyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical; and
R_6 and R_7 are each independently H, methyl, methoxy, or ethoxy.

25. A method for treating a patient with a central nervous system disorder, said method comprising administering to the patient a pharmaceutically-effective amount of a compound of formula (I)B.

26. A method of claim 25, wherein said central nervous system disorder is selected from sleep/wake disorders, arousal/vigilance disorders, dementia, Alzheimer's disease, epilepsy, narcolepsy, eating disorders, motion sickness, vertigo, attention deficit hyperactivity disorder, learning and memory disorders, mild cognitive impairment, and schizophrenia.

27. A method of claim 25, wherein said disorder is selected from sleep/wake disorders, arousal/vigilance disorders, attention deficit hyperactivity disorder, and learning and memory disorders.

28. A method of claim 25, wherein said compound has a formula wherein: one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, and halo;
R_a and R_d are each independently H or methyl;
W is -O- or C_{1-3} alkoxy;
Z is pyrrolidino, N-methylpyrrolidino, pyridyl, thiazoyl, piperidino, N-methylpiperazino, or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-2} alkyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical; and
R_6 and R_7 are each independently H, methyl, methoxy, or ethoxy.

29. A method of claim 25, wherein said compound has a formula selected from 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]-phenyl)-1H-indole; 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]-phenyl)-1-(methylsulfonyl) -1H-indole; 2-[4-[3-Piperidino-propoxy]phenyl)-1H-indole; 2-[4-[3-Piperidinopropoxy]-phenyl)-1-(methylsulfonyl)-1H-indole; 2-[3-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole; 2-(4-(3-(4-methylpiperazino)propoxy)-phenyl)indole; and 1-(methylsulfonyl)-2-(4-(3-(4-methylpiperazino)-propoxy)phenyl)indole; or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.

30. A method for treating a patient with an upper airway allergic response, said method comprising administering to the patient a pharmaceutically-effective amount of a compound of formula (I)B.

31. A method of claim 30, wherein said compound has a formula wherein: one of R_b, R_c, and R_e is WZ and the others are independently selected from H, methyl, ethyl, methoxy, ethoxy, amino, and halo;
R_a and R_d are each independently H or methyl;
W is -O- or C_{1-3} alkoxy;
Z is pyrrolidino, N-methylpyrrolidino, pyridyl, thiazoyl, piperidino, N-methylpiperazino or $NR_{11}R_{12}$ where each of R_{11} and R_{12} is independently selected from H, C_{1-2} alkyl, phenyl, benzyl, C_{3-8} cycloalkyl, and C_{2-5} heterocyclic radical; and
R_6 and R_7 are each independently H, methyl, methoxy, or ethoxy.

32. A method of claim 30, wherein said compound has a formula selected from 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1H-indole; 2-[4-[2-[1-(methyl)-2-pyrrolidinyl]ethoxy]phenyl)-1-(methylsulfonyl) -1H-indole; 2-[4-[3-Piperidinopropoxy]phenyl)-1H-indole; 2-[4-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole; 2-[3-[3-Piperidinopropoxy]phenyl)-1-(methylsulfonyl)-1H-indole; 2-(4-(3-(4-methylpiperazino)propoxy)-phenyl)indole; and 1-(methylsulfonyl)-2-(4-(3-(4-methylpiperazino)-propoxy)phenyl)indole; or a pharmaceutically acceptable salt, amide, ester, or hydrate thereof.